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SAXS Study of Protein Cold Denaturation

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We present the first comprehensive study of the cold denaturation of proteins using small-angle x-ray scattering (SAXS). The radius of gyration of equine cytochrome-c is determined at varying salt conditions from -25 to 60°C and compared to a two-state model. The incorporation of a temperature-dependent pH and solvent dielectric constant is critical to model electrostatic interactions over this broad temperature range and properly predict the observed protein stability from sequence. At suitable conditions, the protein can be made to increase in size by nearly 9 Å (over 60% of its native radius of gyration) when dropped in temperature from 0 to -25°C. This result is promising for future studies of ultrafast protein folding using time-resolved SAXS where initially cold denatured protein will be suddenly jumped in temperature by an infrared laser to initiate folding.